

Remarks/Arguments

Favorable consideration of this application is respectfully requested in view of the foregoing amendment and the following remarks.

Amendment to the Claims

Claims 7, 16-18 are pending in the application

Claim 7 is amended to remove reference to a commercial database and include additional features presented in Examples 8-10

Claim 16-18 are amended for consistency with claim 7 from which they depend.

No new matter has been added

35 U.S.C. § 112, 2nd paragraph

The Examiner has rejected claim 7 as being indefinite because it refers to the commercial database, Accession No: NM005282. Claims 16-18 are also rejected as dependent claims from claim 7.

The rejection is rendered moot as claim 7 has been amended to remove reference to NM005282. In view of the foregoing, applicants request that the rejection be reconsidered and withdrawn.

35 U.S.C. § 102 (e)

Yang et al.

The Examiner has rejected Claims 7, 17, and 18 under 35 U.S.C. 102(e) as being anticipated by Yang et al. (US Patent No. 6,919,176 B2). The examiner states that Yang et al. teach a human G-protein coupled receptor 4 that is 98.7% identical to the amino acid sequence set forth in SEQ ID NO: 3. The Examiner further states that Yang et al. teach screening assays for determining inhibitors and activators of the GPCR by measuring a variety of signals, such as second messenger. The Examiner concludes that the teachings of Yang et al. meet the limitations of Claims 7, 17, and 18. Applicants disagree and traverse the rejection.

The Claims have been amended to require a selection of pH to simulate GPR4. The Applicants have identified in the present application that an appropriate pH must be selected in the assay in order to activate the GPR4 receptor signal. This is clearly illustrated by the Applicants in Examples 9 & 10, where the selection of pH in the range of 6.8-7.0 was shown to produce maximal stimulation of GPR4. The Applicants were the first to discover and disclose that pH stimulates GPR4; thus, Yang et al. does not and could not teach the selection of an appropriate pH to stimulate GPR4. Because Yang et al. does not teach each element of the amended claims, Yang et al. does not anticipate the claims.

In addition, the disclosure of Yang et al is not sufficient to enable the development of screening assays for identifying modulators (agonists or antagonists) of GPR4 signaling as claimed in the present invention.

In order to develop screening assays to identify modulators of GPR4 signaling, one must be able to: 1) stimulate (or activate) GPR4 signaling, and 2) measure the GPR4 signaling activity by known downstream effectors, i.e.: 2nd messenger produced by stimulation of GPR4. The first step requires knowledge of the specific stimuli or natural ligand of GPR4, while the second step requires knowledge of a specific readout associated with the specific stimulus.

The Examiner has cited passages from Yang et al. referring to possible screening assays for GPCR activity (columns 33, 34, and 35), however the Applicants point out that Yang et al. does not teach or suggest a specific stimulus or ligand that could be used to stimulate GPR4 signaling. The Applicants have discovered for the first time that GPR4 "*responds to pH shifts*" (Example 9) and this range has an upper and lower limit at which receptor signaling is active (Examples 2 & 9).

Thus, not only would one skilled in the art not have derived the specific ligand from Yang et al. one would not have known to select a specific pH to elicit the pH dependant stimulation of GPR4. The Applicants assert that since Yang et al. did not identify a specific stimulus, thus they would not have known the appropriate conditions to stimulate GPR4 signaling activity which allow for identification of candidate compounds that modulate GPR4 and, therefore, does not enable the claimed invention.

Logan et al.

The Examiner has also rejected Claims 7, 17, and 18 under U.S.C. 102(e) as being anticipated by Logan et al. (US 2003/0109044 A1). The Examiner states that Logan et al. teach a human G-protein coupled receptor, 279, which is 98.7% identical to the amino acid sequence set forth in SEQ ID NO: 3 along with screening assays for identifying modulators that bind 279 receptor or have a stimulatory or inhibitory effect on 279 receptor activity (page 24, paragraph [0282]). Applicants disagree and traverse the rejection.

As stated above, the Claims have been amended to require a selection of pH to simulate GPR4. The Applicants were the first to identify in the present application that an appropriate pH must be selected in the assay in order to activate the GPR4 receptor signal. This is clearly illustrated by the Applicants in Examples 9 & 10, where the selection of pH in the range of 6.8-7.0 was shown to produce maximal stimulation of GPR4. The Applicants were the first to discover and disclose that pH stimulates GPR4. Thus, Logan et al. does not and could not teach the selection of an appropriate pH to stimulate GPR4. Because Logan et al. does not teach each element of the amended claims, Logan et al. does not anticipate the claims.

In addition, the disclosure of Logan et al. is not sufficient to enable the development of screening assays for identifying modulators (agonists or antagonists) of GPR4 signaling as claimed in the present invention.

In order to develop screening assays to identify modulators of GPR4 signaling, one must be able to: 1) stimulate (or activate) GPR4 signaling, and 2) measure the GPR4 signaling activity by known downstream effectors, i.e.: 2nd messenger produced by stimulation of GPR4. The first step requires knowledge of the specific stimuli or natural ligand of GPR4, while the second step requires knowledge of a specific readout associated with the specific stimulus.

The Examiner has cited passages from Logan et al. referring to general cell based screening assays. The Examiner states that Logan et al. (page 25, paragraph [0289]) teach screening a cell based assay in which a cell expressing 279 receptor is contacted with a test compound and the ability of the test compound to modulate the activity of the 279 receptor is determined by monitoring biological messengers or G-protein signaling. The Applicants point out that Logan et al. do not teach nor suggest a specific stimulus or ligand that could be used to stimulate a GPR4 signal, therefore the first step of selecting pH conditions which stimulate GPR4 signaling is not enabled by Logan et al. The Applicants have discovered for the first time that GPR4 "*responds to pH shifts*" (Example 9). Logan et al. does not teach a specific ligand for GPR4, or the appropriate assay conditions which must be selected to stimulate GPR4 and thereby determine whether a candidate compound is able to increase or decrease pH-dependent stimulation of GPR4. Therefore, Logan et al. does not enable the claimed invention.

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the present application. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,


Karen A Lacourse
Agent for Applicant
Reg. No. 53,175

Novartis Institutes for Biomedical Research, Inc.
220 Massachusetts Ave.
Cambridge, MA 02139
Phone: 617-871-3040

Date: February 23, 2010